Citation:

Fujioka K, Greenway F, Sheard J, Ying Y. The effects of grapefruit on weight and insulin resistance: Relationship to the metabolic syndrome. *J Med Food*. 2006 Spring; 9 (1): 49-54.

PubMed ID: 16579728

Study Design:

Randomized trial

Class:

X - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To look at the effects of whole grapefruit, grapefruit juice and grapefruit juice extract on weight andmetabolic syndrome.

Inclusion Criteria:

- Male and females with a body mass index (BMI) between 30 and 40 kg/m^2
- Stable weight within a 3kg range in the three months prior to the study
- Willing to eat grapefruit daily and willing to avoid other citrus products during the study.

Exclusion Criteria:

- Uncontrolled hypertension
- Type 1 or type 2 diabetes, gastrointestinal surgery for obesity, moderate to severe gastrointestinal disorders, chronic renal disease or cardiovascular disease
- Known liver disease (patients with increased liver function tests who were asymptomatic were included in the study)
- Using cholesterol medications, planning to change smoking status or using medications known to interact with grapefruit
- For those using replacement estrogen or thyroid hormones, on a stable dose for less than four months
- Positive pregnancy test at the the start of the study for those of child-bearing potential.

Description of Study Protocol:

Recruitment

Subjects were recruited through print advertisement and flyers in the rooms of primary care physicians.

Design

12-week, four-arm, double-blinded, placebo-controlled randomized trial

Dietary Intake/Dietary Assessment Methodology

Not used.

Blinding Used

Double-blinded.

Intervention

- Four arms (juice and capsules or placebo were consumed three times a day before each meal:
  - Grapefruit capsule group: Grapefruit capsules and 7 ounces of apple juice
  - Placebo group: Placebo capsules and 8 ounces of grapefruit juice
  - Grapefruit juice group: Placebo capsules and 8 ounces of grapefruit juice
  - Grapefruit group: One-half of a fresh grapefruit and placebo capsules
- Juice was supplied in individual servings and subjects were given a two- to four-week supply at a time
- Subjects were asked to continue on their usual diet
- Subjects were encouraged to walk 20-30 minutes three or four times a week
- Subjects were seen monthly for three months.

Statistical Analysis

- Tukey's studentized range test was used to test for differences in weight, waist and BMI
- The chi-square test was used to test for differences in race and gender
- A mixed model was used to analyze the outcomes, weight, blood pressure and laboratory data
- Analysis of variance and general linear models were used to analyze demographic data.

Data Collection Summary:

Timing of Measurements

- After screening, subjects were seen monthly for three months
- Body weight and blood pressure were obtained at each visit
- Fasting blood samples were obtained at screening, at randomization, and at the final visit at the end of month three (electrolytes, blood urea nitrogen, liver function tests, lipids and complete blood count)
- Two-hour glucose tests with insulin assays were done at the start of the study and on the final visit.

Dependent Variables

- Body weight
- Blood pressure
- Waist circumference (WC)
- High-density lipoprotein (HDL)
- Triglycerides (TG)

- Insulin
- Fasting glucose
- Glucose tolerance (two-hour insulin).

Independent Variables

- Four diet arms:
  - Grapefruit capsule group
  - Placebo group
  - Grapefruit juice group
  - Grapefruit group.

Control Variables

None.

Description of Actual Data Sample:

- *Initial N:* 91
  - 74 females
  - 17 males
- *Attrition (final N):* 77
- *Age:* Not reported
- *Ethnicity:* 76% Caucasian
- *Other relevant demographics:* None
- *Anthropometrics:* Mean BMI was 35.6 kg/m^2; 31 subjects had metabolic syndrome
- *Location:* United States.

Summary of Results:

Key findings

- Weight loss in the fresh grapefruit group (1.6kg) was significantly greater compared to placebo (0.3 kg) after 12 weeks of treatment (P=0.048)
- There was a significant decrease in two-hour insulin in the grapefruit group compared to the grapefruit capsule group (P=0.046).

Changes Over 12-weeks of Treatment

Variables	Treatment Group Capsule	Control Group Placebo	Treatment Group Juice	Treatment Group Fruit
Body weight loss (kg)	1.1	0.2	1.5	1.6

Other Findings

For the 31 subjects with metabolic syndrome, there was significantly more weight loss in the grapefruit capsule group (P= 0.02), the grapefruit capsule group (P=0.017), and the fresh

grapefruit group (P=0.04) compared to the placebo group. In addition, two-hour insulin dropped significantly more in the grapefruit juice group compared with the grapefruit capsule group (P=0.01) and dropped more in the fresh grapefruit group compared to the grapefruit capsule group (P=0.01) and the placebo group (P=0.037).

Author Conclusion:

Eating half a fresh grapefruit before each meal three times a day is associated with weight loss over three months in obese subjects.

Reviewer Comments:

***Study strengths**:*

- *Four arms with placebo control*
- *Double-blinded.*

***Study limitations**:*

Did not measure treatment diet adherence or caloric intake.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	???
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	Yes
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	No
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes